AD-A106 825 AIR FORCE INST OF TECH WRIGHT-PATTERSON AFB OH F/G 6/5
FELINE MALIGNANT LYMPHOMA: A MULTIWAY FREQUENCY ANALYSIS OF A P--ETC(U)
JUL 79 M V SLAYTER
UNCLASSIFIED AFIT-CI-79-300T-5 NL

END
DATE
FILMED
8
DTIC

UNCLASS

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE

READ INSTRUCTIONS BEFORE COMPLETING FORM

1. REPORT NUMBER: 79-300T-S (6)	2. GOVT ACCESSION NO.: AD-A106825
3. RECIPIENT'S CATALOG NUMBER	
4. TITLE (and Subtitle): Feline Malignant Lymphoma: A Multiway Frequency Analysis of a Population Involving Sex, Age, Cell Type, and Tumor Location.	5. TYPE OF REPORT & PERIOD COVERED: THESIS/~~DISSERTATION~~
	6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s): Capt Michael V. Slayter (10) (1)	8. CONTRACT OR GRANT NUMBER(s)
9. PERFORMING ORGANIZATION NAME AND ADDRESS: AFIT STUDENT AT: Univ of California - Davis	10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS: (11) (12) 31
11. CONTROLLING OFFICE NAME AND ADDRESS: AFIT/NR WPAFB OH 45433 (7)	12. REPORT DATE: Jul 1979
	13. NUMBER OF PAGES: 15
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office): (14) AFIT-CI-79-300T-5	15. SECURITY CLASS. (of this report): UNCLASS
	15a. DECLASSIFICATION/DOWNGRADING SCHEDULE

LEVEL II

16. DISTRIBUTION STATEMENT (of this Report)

APPROVED FOR PUBLIC RELEASE; DISTRIBUTION UNLIMITED

DTIC ELECTE NOV 9 1981 D

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

H

27 OCT 1981

18. SUPPLEMENTARY NOTES

APPROVED FOR PUBLIC RELEASE: IAW AFR 190-17

Fredric C. Lynch

FREDRIC C. LYNCH, Major, USAF
Director of Public Affairs
Air Force Institute of Technology (ATC)
Wright-Patterson AFB, OH 45433

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

ATTACHED

DD FORM 1 JAN 73 1473 EDITION OF 1 NOV 65 IS OBSOLETE

UNCLASS 012200

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

81 11 03 041

AD A106825

DTIC FILE COPY

SUMMARY

A multidimensional descriptive study of feline malignant lymphoma was performed using age, sex, cell type, and tumor location of 1,733 cases. The interactions between these four variables were determined and interpreted. Particular consideration was given to the relationships of age to tumor location, age to sex, and tumor location to cell type. These three interactions were shown to be the major interactions in the study. The use of computer analysis of the multiway frequency table was discussed. Suggestions were offered that future lymphoma studies utilize the multiway frequency table with different variables.

79-3001-S

FELINE MALIGNANT LYMPHOMA: A MULTIWAY FREQUENCY ANALYSIS OF A POPULATION INVOLVING SEX, AGE, CELL TYPE, AND TUMOR LOCATION

by

Michael V. Slayter, D.V.M.

Submitted in Partial Fulfillment
of the Requirements for the Degree of

MASTER OF PREVENTIVE VETERINARY MEDICINE
(MPVM)

Department of Epidemiology and Preventive Medicine
School of Veterinary Medicine

UNIVERSITY OF CALIFORNIA, DAVIS
California 95616, U.S.A.

July 1979

Reviewed and Approved by

Robert Schneider

Robert Schneider
Associate Adjunct Professor

Thomas B. Farver

Thomas B. Farver
Assistant Professor of Biostatistics

Dedication

To my wife, Jane. Thanks for your patience.

To Dr. Thomas E. Vice, San Antonio, Texas. Thanks for setting the example so many years ago.

Acknowledgements

I would like to thank Dr. Thomas Farver, Dr. Robert Schneider, and the staff of the Animal Neoplasm Registry for their continued support and encouragement.

SUMMARY

A multidimensional descriptive study of feline malignant lymphoma was performed using age, sex, cell type, and tumor location of 1,733 cases. The interactions between these four variables were determined and interpreted. Particular consideration was given to the relationships of age to tumor location, age to sex, and tumor location to cell type. These three interactions were shown to be the major interactions in the study. The use of computer analysis of the multiway frequency table was discussed. Suggestions were offered that future lymphoma studies utilize the multiway frequency table with different variables.

Introduction

Characteristics within a diseased population can sometimes help to define the disease itself. These characteristics or variables rarely, if ever, exist without some mutual association to each other or to other variables. In using these associations or interactions as a foundation for a biological hypothesis, the total picture becomes more complete if one examines all interactions simultaneously. Using many variables in a descriptive study tends to emulate nature more closely, but the issue of explaining the interactions becomes more difficult if too many variables are used. Since data in general has a quality of randomness, it follows that the more variables examined in a population study, the larger the sample size should be to assure adequate representation of those variables.

Malignant lymphoma is considered the most frequently occurring cancer in cats.[6,15] It is associated with a virus, Feline Leukemia Virus (FeLV).[2,12] Since its discovery, two other viruses have come to be recognized as close relatives of FeLV. Feline cellular DNA has been shown to have certain parts of its genetic code in common with the genomes of these viruses,[12] hence the place of FeLV in the etiology of feline malignant lymphoma is not clear. Studies of household clusters have been made which both support[7] and refute[21] the idea of horizontal transmission of the disease.

The age related incidence rate of the disease is bimodal, peaking at around 2 and 10 years.[22] Males have a two-fold excess in incidence over females. Males peak in incidence at about 7 years of age. Females peak at about 1 year.[22] According to some, malignant lymphoma has certain distinct cell types.[6,15,19,23] Others feel the various types are manifestations of the same cell, but simply in different stages of maturation.[6,15,23] From the standpoint of tumor location, the internal form (visceral) is much

more common in cats than the multicentric or solitary forms.[15]

Investigations about single characteristics of a disease at any given time are valuable, but only reveal part of the total biological interactions. A method of simultaneous examination of numerous variables exists using a multiway frequency table.[3,5] This study presents such a multidimensional analysis using the multiway frequency table. The variables involved were age, cell type, sex, and tumor location.

Methods and Materials

All computer procedures in this study were done using BMDP7D, BMDP3F, and TUSTAT 11 'chi square'. The study was conducted using the records of the Alameda/Contra Costa Animal Neoplasm Registry. A complete description of this registry is presented in the literature.[20] Tumor submissions were used from the period of January 1970 to December 1978. A total of 2,437 cases were submitted during that period. Each case was categorized by sex (neutered feamle; female; neutered male; male), age in years, tumor location (abdominal; thoracic; multicentric),[15] and cell type (lymphocytic-well differentiated; lymphocytic-poorly differentiated; histiocytic).[17] Seven hundred nine cases did not have complete information available pertaining to the variables involved. Most of the missing information concerned cell types. To test for randomness of these cases, an analysis of variance was performed (using BMDP7D) comparing the mean ages of the cases grouped by the three cell types. Those without a specified cell type were designated as a fourth cell type group. This analysis showed that the non-specific group did not differ from the others in terms of mean age. It was judged from this that the non-specific cell type cases were randomized sufficiently to allow for their disposal without biasing the complete data set.

Age was then transformed into a discrete variable having three levels. These levels were 0-4 years, 5-8 years, and 9 years or older. These intervals represent young, mid-age, and old animals, respectively, and represents the two peaks and the trough of the bimodal age-related incidence.[22]

After age had been transformed, the multiway frequency table was created and is shown in Table 1. It consisted of 108 cells, all of which had non-zero frequencies except for five of them. To guarantee that no cell would have an expected value of zero, a fictitious frequency of 1 was inserted into each

of these five cells. It seemed intuitive that these five cases would not alter the final conclusions. The multiway frequency table now had 1,733 cases.

In the work presented here, the following codes were used to designate the variables:

(A) age (S) sex (C) cell type (L) tumor location

Analysis of the multiway frequency table employed the use of BMDP3F.[3,5]

This particular program tests for association of all possible combinations of the variables (bivariate and more complex). In the planning stages, the rule of thumb is the total frequency count must be at least 10 times the number of cells in the table. Using too many levels for each variable would increase the number of cells and possibly cause the investigator to violate this rule.

For each model fit, the program prints a goodness of fit statistic, G^2. This statistic, for large samples, is asymptotically equivalent to the familiar Pearson Chi square statistic. G^2 is calculated as:

$$2 \sum_{\text{cells}}^{\text{all}} (\text{observed}) \log \frac{(\text{observed})}{(\text{expected})}$$

Recall the Pearson Chi square is:

$$\sum_{\text{cells}}^{\text{all}} \frac{(\text{observed-expected})^2}{\text{expected}}$$

G^2 is computed initially for the complete independence model, which is (A) (S) (L) (C) in this study. The G^2 value was then computed for each model of increasing complexity up to the completely saturated model, (ASLC). As the models tested become more complex, the G^2 value becomes smaller indicating a somewhat better fit. The changes in G^2 between adjacent models, with appropriate degrees of freedom, are inspected for significance using a Chi

square distribution table.

In order to quickly focus in on several models which might be the appropriate one, and at the same time, eliminate those that warrant no consideration, the program provided a G^2 for the complete independence model, (A) (S) (C) (L); the all possible second order interactions model, (AS) (AC) (AL) (SC) (SL) (CL); and the all possible third order interactions model, (ASC) (ASL) (ACL) (SCL). The program indicated the independence model did not provide a good fit for the data, but the others did. Subsequent efforts toward finding the simplest model with a good fit consisted of fitting models between the complete independence model and the all possible second order interactions model.

Finding the best fitting model can be done using a forward or backward stepwise procedure. In the present analysis, the forward stepping procedure started with the complete independence model. At each step a two-factor interaction was added to the model. The two-factor interaction selected was that which produced the most significant reduction in the size of the G^2 obtained for the model of the previous step. The selection procedure stopped at that step when no remaining two-factor interaction could produce a statistically significant reduction in the size of G^2. The backward elimination procedure started with the all possible second order interactions model. Two-factor interactions were removed individually in a stepwise fashion if removal failed to produce a statistically significant increase in the G^2 obtained from the previous step. The two-factor interaction selected for removal at each step was that which made the least impact on the G^2 value.

Once a model was selected, the next hurdle was that of interpreting each interaction. Since the final model contained nothing higher than second order interactions (bivariate), the interpretation was enhanced by collapsing the four-way frequency table to a series of two-way frequency tables and

performing the respective two dimensional tests for association. One-way analysis of variance was used as an additional tool in interpreting the results. When statistically significant results were observed with the analysis of variance, Scheffe's procedure for multiple pairwise comparison was used.[19] The formula for this comparison is:

$$F = \frac{\bar{X}_1 - \bar{X}_2}{(K-1)\ (MSW)\ \left(\frac{1}{n_1} + \frac{1}{n_2}\right)}$$

where n is the number of cases in each group

K is the number of groups

MSW is the mean square within (from the ANOVA table)

N is the total number of cases

$\bar{X}$ is the mean age for each group

(This F statistic is considered significant and rejects the assumption of equality between the two groups tested if it exceeds the tabulated F value with (K-1) and (N-K-1) degrees of freedom.)

Results

Models involving the third and fourth order interactions were excluded from consideration after the initial screening. The G^2 for the all possible second order interactions model was insignificant indicating a good fit. One might be inclined to stop here. However, if there was a simpler model with a good fit, the investigator is obliged to look for it.

With the present data, a slight inconsistency emerged in the forward stepping procedure. The search for the model went through five steps, yielding one of two models:

(AL) (AS) (LC) (SC) (AC) (1)

and

(AL) (AS) (LC) (AC) (SL) (2)

Two models were indicated because the decision at step 4 between inclusion of (SC) or (SL) was too close to call.

Using the backward stepping procedure, the selection stopped after (SC) was removed, yielding model (2) above. In light of this uncertainty, one might be inclined to use either model above or the model with all six interactions:

(AL) (AS) (LC) (AC) (SL) (SC) (3)

It should be pointed out that major reduction in G^2 at step 1 of the forward stepping procedure could have been made by including any of the interactions, (AL), (AS), or (LC) in the model. In fact, after three steps, these three interactions were all included in the model. The point being that these are the strongest interactions in the final model. The remaining three second-order interactions were of a lower magnitude as shown by their lesser impact on G^2 at step 1.

Regardless of which of the three models seems appropriate, explanation or interpretation of each second-order interaction in the model is the next logical step. Tables 2-7 attempt to do this with two-way Chi square tests for association.[13] The purpose of these tables was to show how the levels of one variable relate to the levels of another variable. Each cell of Tables 2-7 is bisected with a diagonal line. The number above that line is the observed frequency for that cell. The number below that line is the ratio of observed frequency:expected frequency. In many of the tables, a pattern can be seen in a row-wise or column-wise fashion. In Table 2, rows 1, 3, and 4 show observed frequencies that do not stray that much from the expected frequency (as evidenced by the observed:expected ratio being close to 1) with the exception of the neutered male/thoracic cell. Row 2, however, is inconsistent with the rest of the table by having frequencies less than expected in the first two cells, and more than expected in the last cell. It is this inconsistency that produces the significant association. If the three tumor locations in Table 2 had the same frequency pattern regardless of the level of sex, it could be stated that neither variable affected the other. Hence, there would be no association.

More specifically, Table 2 indicates that female patients tend to have more thoracic tumors than expected and less abdominal and multicentric tumors than expected. Reconstructing a similar table without the female row results in an insignificant Chi square value. There was a less than expected frequency of thoracic/neutered male patients, but not enough to cause a detectable inconsistency.

Table 3 indicates the intact females had a less than expected frequency of histiocytic cell type, and an abundance of the other two cell types. In a manner similar to Table 2, Table 3 can be made to have no inconsistencies (and consequently, a non-significant Chi square value) by removing the

Female row.

Tables 4, 5, and 7 represent the interactions which had a strong impact on the G^2 statistic during the forward stepping procedure. Table 4 shows the thoracic/histiocytic cell had only about half its expected frequency. The other two cell types seem to have substantially more than their share in the thoracic category.

In Table 5, the association is also strong but somewhat more difficult to interpret. Removal of the first column and last row was required to produce a non-significant matrix. Perhaps the interest should lie with those cells having observed:expected ratios substantially different from 1. There is an abundance of old abdominal and young thoracic patients and a shortage of mid-age and old thoracic patients.

Table 7 illustrates an interesting fact. A non-significant matrix was produced by removing rows 1 and 3, the two neutered rows. The pattern of the two intact rows was that of an abundance in the first column and a shortage in the other two columns. Not only was the pattern of the two neutered rows dissimilar to the intact rows, they were dissimilar to each other.

In Table 6, the pattern for the first and third rows seems to show an abundance in the first cell and a shortage in the last cell. The histiocytic row reverses this pattern.

Analysis of variance was also used to illustrate the relationship between age and the other three variables. In order to do this, age was treated in its original form, that of a continuous variable. In Table 8, the analysis of variance indicated an inequality somewhere between the group mean ages. Employing pairwise multiple comparisons,[19] the histiocytic group proved to have a mean age unequal to the others. In this case the histiocytic group was approximately one year older than the other two.

Summarizing Table 9, each tumor location group had a statistically different mean age from the other two groups. Thoracic tumor patients were the youngest, abdominal tumor patients were the oldest, with multicentic in between.

The analysis of variance was also significant in Table 10. Pairwise comparison of the groups indicated the two intact groups shared a common age, and the two neutered groups also had equal mean ages. A contrast then revealed that the common mean age of the intact groups was different from the common mean age on the neutered groups. Such contrasts are formed by a Scheffe's confidence interval[19] of the form:

$$\frac{\bar{X}_1 + \bar{X}_2}{2} - \frac{\bar{X}_3 + \bar{X}_4}{2} \pm \sqrt{(K-1)\,(MSW)\left[F_{K-1,\, N-K,\, 1-\alpha}\right] \sum_{i=1}^{K} \frac{C_i^2}{N_i}}$$

where C_i^2 represents the square of the weight for a given group in the contrast.

Discussion

The first fact that emerged from the BMDP3F program application was that there were no third order interactions in the model. Thus, each bivariate combination had a particular pattern which did not depend on any given level of a third variable.

It is a general impression among many observers that most young cats with lymphoma show involvement of the anterior mediastinum or thymus.[6] Table 5 shows there are more young thoracic patients than is expected, as evidenced by the increased observed:expected ratio in that particular frequency cell. Perhaps the development of abdominal or multicentric lymphoma requires longer exposure to certain agents and/or environmental factors; something which can only come with age. In fact, there is a definite abundance of old abdominal cases and a much less than expected number of old thoracic cases. Since the terms young, mid-age, and old have different definitions in various situations, the biomodal age peaks mentioned earlier were used as guides for the transformation of age from a continuous variable to a discrete variable. In the analysis, age produced a significant Chi square value (as a discrete variable) as well as a significant F ratio (as a continuous variable) when it was cross classified with each of the other three variables. This supports the choice of age intervals used in the transformation.

In examining the effect of sex on the other three variables, it was found that sex does not assume a male/female effect (Tables 7 and 10), but rather a neutered/intact one. According to Table 10, neutered animals were approximately two years older than intact animals at the time of diagnosis. Feline mortality data collected by the animal neoplasm registry indicates that lifespan appears to be biologically extended in neutered cats. Therefore, it is possible that either the disease starts later in neutered animals, or

progresses slower in such animals. On the other hand, assuming the disease is of an infectious nature, it has been suggested that transmission of the disease may be linked to sexual activity which could be explained by the close and frequent contact between unaltered animals. In Table 2 and 3, the sex effect was that of intact female vs all other sex categories. Perhaps if a third order interaction had occurred in the model, some light would be shed as to why the intact female group stands in contrast with the other three sex categories when cross classified with cell type and tumor location.

Tables 2, 4, 5, and 9 indicate that thoracic tumors are totally or partly involved in the statistical significance of each respective table. This might be a reflection of T cell activity. One study has shown multicentric and thymic (thoracic) lymphoma to involve primarily the paracortical and thymus-dependent areas (T cell) of lymphoid tissues.[14] FeLV is known to have an influence on the immune response system as indicated by increased allograft retention time.[16,2] These facts are supportive for future multidimensional studies which involve B vs T cell as one of the variables. Indicator systems for identifying B and T cell are described in the literature.[9,1]

The Rappaport classification[17] shows histiocytic and lymphocytic cell types as having separate developmental pathways. Throughout this study, with only one exception (Table 6, middle column), the histiocytic cell type was contrasted with the other two cell types. This is seen when examining the observed:expected ratios contained in Tables 3, 4, and 6. In Table 8, the mean age of the histiocytic group is significantly different from the other two. Recall that tumor location:cell type (LC) made a strong entry into the model. In Table 4, the observed:expected ratios indicate a shortage of histiocytic-thoracic patients. If one accepts the idea of the three cell types being stages of the same cell, this shortage could be due to the cells developing faster in the thoracic cavity, giving the diagnostician less chance to see the histiocytic form at that site. On the other hand, if one does not

accept the developmental idea, most of the thoracic cases could be considered thymus-dependent, which would preclude them from being histiocytes. Caution must be exercised about making hard and fast statements about cell types, however, since such classification are many times a subjective matter.

The multidimensional model might suggest the interaction of viral subgroups.[11,18] One study suggests that no correlation exists between viral types and tumor locations.[11] Another study suggests correlation of geographical area and tumor location.[4] Still other studies[10,8] suggest the viral types have affinity for different cell populations. A three dimensional study using a multiway frequency table could show interactions, if any exist, between viral type, tumor location, and geography.

One could speculate at length about all the possible reasons for various interactions in the model here. It might be appropriate to accept the model at face value and attempt to find similar patterns in other species.

Conclusion

The three main interactions found in the study were age and tumor location, age and sex, and tumor location and cell type. These interactions pointed out that (1) age and tumor location may show some association with B or T cell activity, (2) the effect of sex on age is expressed in terms of neutering, and (3) thoracic lymphoma tends to be lymphocytic in general rather than histiocytic. The distributions and interactions lend strength and support to the concepts of both vertical and horizontal transmission. Additional questions are also posed by the data which could lead to further studies concerning etiology, sex effects, and immunologic aspects.

TABLE 1

Multiway frequency table of 1,753 cases of feline lymphosarcoma grouped by age, sex, cell type and tumor site.

Site	Cell	Sex	Age Young	Age Middle	Age Old
Mult	Well	NF	30	6	10
		F	18	4	2
		NM	28	13	7
		M	32	2	2
	Hist	NF	51	13	17
		F	26	4	4
		NM	70	36	31
		M	49	11	14
	Poor	NF	17	8	6
		F	19	5	1
		NM	28	26	12
		M	25	8	2
Abd	Well	NF	17	7	12
		F	11	2	6
		NM	23	19	18
		M	23	3	4
	Hist	NF	28	22	31
		F	27	6	8
		NM	67	57	36
		M	44	21	16
	Poor	NF	18	8	12
		F	25	2	8
		NM	40	17	17
		M	30	5	4
Thor	Well	NF	25	2	2
		F	38	1	1
		NM	34	6	2
		M	32	4	1
	Hist	NF	16	3	5
		F	15	2	1
		NM	21	8	2
		M	20	1	1
	Poor	NF	31	3	2
		F	28	6	1
		NM	36	13	3
		M	17	9	2

TABLE 2

Bivariate relationship of tumor location to sex. Number above diagonal in a given cell is the observed frequency. The number below the diagonal is the ratio of observed frequency:expected frequency.

SEX	LOCATION: Multicentric	LOCATION: Abdominal	LOCATION: Thoracic
Neutered Female	158 / 1.069	155 / .963	89 / .954
Female	83 / .833	95 / .875	93 / 1.479
Neutered Male	251 / 1.019	294 / 1.096	125 / .804
Male	145 / 1.011	150 / .960	95 / 1.050

Chi square= 29.0236 with 6 d.f. ($P < .05$)

Removal of second row produces a Chi square of 6.908 with 4 d.f. ($P > .05$)

TABLE 3

Bivariate relationship of sex and cell type. The number above diagonal in a given cell is the observed frequency. The number below the diagonal is the ratio of observed frequency:expected frequency.

SEX	CELL TYPE: Well Differentiated	Histiocytic	Poor Differentiated
Neutered Female	111 / 1.070	186 / 1.023	105 / .902
Female	83 / 1.187	93 / .759	95 / 1.210
Neutered Male	150 / .868	328 / 1.082	192 / .989
Male	103 / 1.024	177 / 1.003	110 / .974

Chi square= 20.0206 with 6 d.f. ($P < .05$)

Removal of second row produces a Chi square of 4.63 with 4 d.f. ($P > .05$)

TABLE 4

Bivariate relationship of cell type and tumor location. The number above the diagonal in a given cell is the observed frequency. The number below the diagonal is the ratio of observed frequency; expected frequency.

CELL TYPE	TUMOR LOCATION Multicentric	Abdominal	Thoracic
Well Differentiated	154 / .937	145 / .810	148 / 1.427
Histiocytic	326 / 1.131	363 / 1.156	95 / .522
Poorly Differentiated	157 / .851	186 / .925	159 / 1.365

Chi square= 100.93 with 4 d.f. (P <.05)

Removal of the thoracic column produces a Chi square of 2.27 with 2 d.f. (P >.05)

TABLE 5

Bivariate relationship of age to tumor location. The number above the diagonal in a given cell is the observed frequency. The number below the diagonal is the ratio of observed frequency; expected frequency.

TUMOR LOCATION	AGE: Young	AGE: Middle Age	AGE: Old
Multricentric	393 / 1.000	136 / 1.025	108 / .970
Abdominal	353 / .824	169 / 1.169	172 / 1.418
Thoracic	323 / 1.303	56 / .669	23 / .327

Chi square= 102.339 with 4 d.f. ($P < .05$)

Removal of first column and last row produces a Chi squire of 2.175 with 1 d.f. ($P > .05$)

TABLE 6

Bivariate relationship of age to cell type. The number above the diagonal in a given cell is the observed frequency. The number below the diagonal is the ratio of observed frequency: expected frequency.

CELL TYPE	AGE: Young	AGE: Middle Age	AGE: Old
Well Differentiated	311 / 1.128	69 / .741	67 / .857
Histiocytic	434 / .897	184 / 1.127	166 / 1.211
Poorly Differentiated	324 / 1.046	108 / 1.033	70 / .798

Chi square= 30.53 with 4 d.f. (P <.05)

Removal of the middle row *or* first column produces Chi square values of 5.752 with 2 d.f. and 4.032 with 2 d.f., respectively (P >.05)

TABLE 7

Bivariate relationship of sex to age. The number above the diagonal in a given cell is the observed frequency. The number below the diagonal is the ratio of observed frequence:expected frequency.

SEX	AGE: Young	Mid-Age	Old
Neutered Female	233 / .940	72 / .860	97 / 1.380
Female	207 / 1.238	32 / .567	32 / .675
Neutered Male	347 / .840	195 / 1.397	128 / 1.093
Male	282 / 1.172	62 / .763	46 / .675

Chi square= 90.35 with 6 d.f. (P <.05)

Removal of rows 1 and 3 (neutered rows) produces a Chi square of 2.24 with 2 d.f. (P >.05)

TABLE 8

Analysis of variance of age grouped by cell type.

Well Differentiated	Histiocytic	Poorly Differentiated
Mean Age 4.054 yrs	Mean Age 5.16 yrs	Mean Age 4.347 yrs
Group Size 446	Group Size 781	Group Size 501
Std. Dev. 3.917	Std. Dev. 4.128	Std. Dev. 3.844

F ratio= 12.775 D.F.= 2,1725

TABLE 9

Analysis of variance of age grouped by tumor location.

Multicentric	Abdominal	Thoracic
Mean Age 4.651 yrs	Mean Age 5.706 yrs	Mean Age 2.753 yrs
Group Size 637	Group Size 694	Group Size 397
Std. Dev. 3.848	Std. Dev. 4.357	Std. Dev. 2.815

F ratio= 73.87 D.F= 2,1725

TABLE 10

Analysis of variance of age grouped by sex category.

Neutered Female		Female		Neutered Male		Male	
Mean Age	5.378 yrs	Mean Age	3.343 yrs	Mean Age	5.328 yrs	Mean Age	3.577 yrs
Group Size	402	Group Size	268	Group Size	670	Group Size	388
Std. Dev.	4.411	Std. Dev.	3.845	Std. Dev.	3.82	Std. Dev.	3.586

F ratio= 30.92 D.F.= 3,1724

REFERENCES

1. Cockerell, G. L., Krokowka, S., Hoover, E. A., Olsen, R. G., Yohn, D. S. Characterization of feline T and B-lymphocytes and identification of an experimentally induced T-cell neoplasm in the cat. J. Natl. Cancer Inst. 57(4):907-913, 1976.

2. Cotter, S. M., Hardy, W. D., Jr., Essex, M. Association of feline leukemia virus with lymphosarcoma and other disorders in the cat. J.A.V.M.A. 166:449-454, 1975.

3. Dixon, W. J., Brown, M. B., eds. BMDP biomedical computer programs p-series. Los Angeles, University of California Press, 880 p., 1977.

4. Essex, M., Cotter, S. M., Hardy, W. D., Jr., Hess, P., Jarrett, W., Jarrett, O., Mackey, L., Laird, H., Perryman, L., Olsen, R. G., Yohn, D. S. Feline oncornavirus associated cell membrane antigen. I.V. antibody titer in cats with naturally occurring leukemia, lymphoma, and other diseases. J. Natl. Cancer Inst. 55(2):463-467, 1975.

5. Fienberg, S. E. The analysis of cross classified categorical data. Cambridge, Mass., MIT Press, 1977.

6. Gilmore, C. E., Holzworth, J. Naturally occurring feline leukemia: Clinical, pathologic, and differential diagnostic features. J.A.V.M.A. 158:1013-1025, 1971.

7. Hardy, W. D., Old, L. J., Hess, D. W., Essex, M., Cotter, S. M. Horizontal transmission of feline leukemia virus. Nature 244(5414):266-269, 1973.

8. Hoover, E. A., Olsen, R. G., Hardy, W. D., Schaller, J. P., Mathes, L. E. Feline leukemia virus infection: Age=related variations in response of cats to experimental infection. J. Natl. Cancer. Inst. 57(2):365-369, 1976.

9. Hoover, E. A., Krokowka, S., Cockerell, G. L., Mathes, L. E., Olsen, R. G. Influence of thymectomy on the susceptibility of cats to feline leukemia virus and lymphosarcoma. Am. J. Vet. Res. 39(6):993-995, 1978.

10. Jarrett, O., Russell, P. H. Differential growth and transmission in cats of feline leukemia virus of subgroups A and B. Int. J. Cancer 21(4):466-472, 1978.

11. Jarrett, O., Hardy, W. D. Jr., Golden, M. C., Hay, D. The frequency of feline leukemia virus subgroups in cats. Int. J. Cancer 21(3):334-337, 1978.

12. Kimball, P. The feline leukemia virus: Currents. Feline Practice 8(2):37-41, March 1978.

13. Koh, Y. O. Tustat II. Reno, Nevada, University of Nevada Press, Chapt. 11, p. 4, 1970.

14. Mackey, L. J., Jarrett, W. Pathogenesis of lymphoid neoplasia in cats and its relationship to immunologic cell pathways. I. Morphologic aspects. J. Natl. Cancer Inst. 49(3):853-865, 1972.

15. Moulton, J. E., Dungworth, D. L. Tumors of the lymphoid and hemopoietic tissues. Chapt. 5, in: Tumors in domestic animals. Moulton, J. E., ed., 2nd ed., University of California Press, pp. 150-196, 1978.

16. Perryman L. E., Hoover, E. A., Yohn, D. S. Immunologic reactivity of the cat: Immunosuppression in experimental feline leukemia. J. Natl. Cancer Inst. 49(5):1357-1365, 1972.

17. Rappaport, H. Atlas of tumor pathology, tumors of the hematopoietic system, Section 3, Fascicle 8, Armed Forces Instititute of Pathology, Washington, D. C., pp. 10-14, 1966.

18. Sarma, P. S.,Log, T. Subgroup classification of feline leukemia and sarcoma virus by viral interference and neutralization tests. Virology 54:160-169, 1973.

19. Scheffe, H. The analysis of variance. New York, N. Y., John Wiley & Sons, 66-72, 1959.

20. Schneider, R. A population based animal tumor registry. Chapt. 17, in: Proceedings of an international symposium on animal disease monitoring held at University of Guelph, July 4-5, 1974, Ingram, D. G., Mitchell, W. R., Martin, S. W., eds. Springfield, Ill., Charles, C. Thomas, publisher.

21. Schneider, R., Frye, F. L., Taylor, D. Dorn, C. R. A household cluster of feline malignant lymphoma. Cancer res. 27:1316-1322, 1967.

22. Schneider, R. Comparative epidemiological aspects of naturally occurring malignant lymphoma in domestic cats and rhesus monkeys. Proceedings of the 7th internation symposium on comparative leukemia research, held in Copenhagen, Denmark, 1975, Clemmensen, J., Yohn, D., eds. Basel, New York: S. Karger, p. 228, 1976.

23. Cell differentiation. In: Vianna, N. J. Lymphoreticular malignancies. Medical and Technical Publishing Co. Ltd., Lancaster England, (p. 7), 1975.

24. Weijer, K. The incidence of lymphosarcoma (leukemia) and feline leukemia virus (FeLV) in cats in The Netherlands (author's travel. Tijdschr Diergeneeskd 100(18):976-986, 1975.